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(54) POUR-ON FORMULATION FOR THE CONTROL OF LICE

(71) WELLCOME AUSTRALIA LIMITED

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(74) GH

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517142

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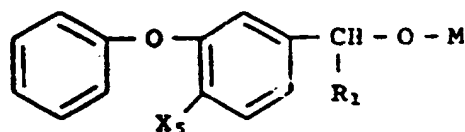
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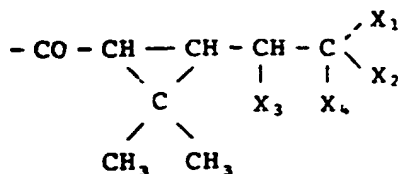
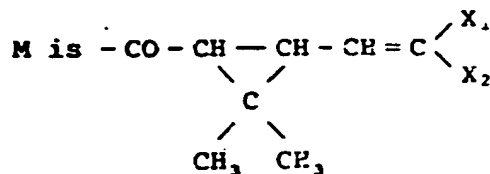
A01N 9/08

(57) Claims

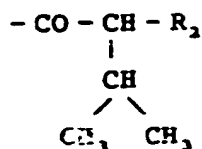
1. A pour-on formulation for localised application,  
which comprises a pyrethroid of the formula



wherein



or



.../2

and wherein  $X_1$  to  $X_n$  are independently selected from halo,  
 $C_1-C_n$  alkyl, halogen-substituted  $C_1-C_n$  alkyl,  
and halogen-substituted phenyl;

$X_n$  is -H or halo;

$R_1$  is -H or cyano; and

$R_2$  is halogen-substituted phenyl;

in admixture with diethylene glycol mono-butyl ether.

APPLICATION ACCEPTED AND AMENDMENT

FORM 1

ALLOWED 16-7-84

21947/83

COMMONWEALTH OF AUSTRALIA

Patents Act 1952-1973

APPLICATION FOR A PATENT

539105

I, We, WELLCOME AUSTRALIA LIMITED

of 53 Phillips Street, Cabarita 2137, New South Wales, Australia

hereby apply for the grant of a Patent for an invention entitled:

"Pour-on Formulation"

which is described in the accompanying complete specification.

... This Application is a separate Application made by virtue of  
 ... sub-section (1) of Section 51 of the Patent Act 1952-1973 in  
 ... respect of an invention disclosed in the complete specification  
 ... in respect of Application No. 91851/82

... Our address for service is care of GRIFFITH HASSEL & FRADER,  
 ... Patent Attorneys of 71 York Street, Sydney 2000, in the  
 ... State of New South Wales, Commonwealth of Australia.

... Dated this 2nd day of December, 1983

WELLCOME AUSTRALIA LIMITED  
 By the Patent Attorneys

GRIFFITH HASSEL & FRADER

TO: THE COMMISSIONER OF PATENTS  
 COMMONWEALTH OF AUSTRALIA

LODGED AT SUB-OFFICE

2 DEC 1983

Sydney

PATENT APPLICANT

COMMONWEALTH OF AUSTRALIA

21947/83

PATENTS ACT 1952 (AS AMENDED)

DECLARATION IN SUPPORT OF AN APPLICATION FOR A PATENT

No. of In support of an Application made by: **WELLCOME AUSTRALIA LIMITED**  
applicant)

Title) for a patent for an invention entitled: **"Pour-on Formulation"**

Full name of I, **ROBERT JUSTIN POWELL**  
signatory) of  
Address of **23 PARK STREET, ESKDALEVILLE, NSW.**  
signatory)

do solemnly and sincerely declare as follows:

1. I am authorised by the above mentioned applicant for the patent to make this Declaration on its behalf.
2. The name and address of each actual inventor of the invention is as follows:

(Insert details of inventor/s)

Peter John Kieran of 3 Bambara Crescent, Beecroft 2119, New South Wales, Australia; and Robert Bruce Townsend, of 40 Edgeworth David Avenue, Waitara 2077, New South Wales, Australia

(Insert details of assignment, etc.)

and the fact(s) upon which the applicant is entitled to make this application are as follows:

applicant is the assignee of the said invention from the said inventors.

(Delete paragraphs 3 and 4 for Non-Convention application)

~~3. The basic application(s) as defined by Section 141 of the Act was(were) made as follows:~~

~~Country ..... on .....  
in the name(s) .....  
and in ..... on .....  
in the name(s) .....  
and in ..... on .....  
in the name(s) .....~~

~~4. The basic application(s) referred to in the preceding paragraph of this Declaration was(were) the first application(s) made in a Convention country in respect of the invention the subject of this application.~~

(Place and date of signing)

Declared at **SYDNEY** this **Twenty** day of **NOVEMBER** 19 **83**

Signed: **ROBERT JUSTIN POWELL**

Position: **MANAGER ADMINISTRATIVE SERVICES**

GRIFFITH HASSEL & FRAZER, P.O. BOX 2133, G.P.O., SYDNEY, N.S.W. 2001 AUSTRALIA



559105

Form 10

PATENTS ACT 1962

**COMPLETE SPECIFICATION**

(ORIGINAL)

FOR OFFICE USE

Short Title:

Int. Cl:

Application Number: 21947/83  
Lodged:

Complete Specification—Lodged:

Accepted:

Lapsed:

Published:

Priority:

Related Art:

This document contains the  
amendments made under  
Section 49

and is correct for printing

Name of Applicant:

TO BE COMPLETED BY APPLICANT  
WELLCOME AUSTRALIA LIMITED

Address of Applicant:

53 Phillips Street, Cabarita 2137, New South  
Wales, Australia

Actual Inventor:

Peter John Kieran and Robert Bruce Townsend

Address for Service:

GRIFFITH HASSEL & FRAZER  
71 York Street  
Sydney, N.S.W. 2000, Australia

Complete Specification for the invention entitled: "Pour-on Formulation"

The following statement is a full description of this invention, including the best method of performing it known to me:—

\* Note: The description is to be typed in double spacing, pica type face, in an area not exceeding 250 mm in depth and 160 mm in width, on tough white paper of good quality and it is to be inserted inside this form.

The present invention relates to a pour-on formulation, particularly for use on merino sheep.

Traditionally, sheep have been treated for the control of ectoparasites by dipping or spraying the whole external surface of the sheep. However, this is an inconvenient and time-consuming and labour-intensive operation. Attempts have been made to treat infested sheep, particularly lice-infested sheep, with a large variety of known insecticides by various other routes, including pour-on treatments, subcutaneous injection, and by oral dosage. Hitherto, none of the treatments had any significant effect on the control of the lice populations. In particular, merino sheep have not responded to such treatments.

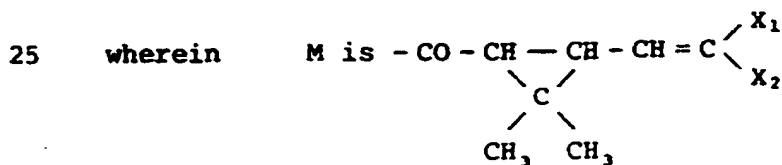
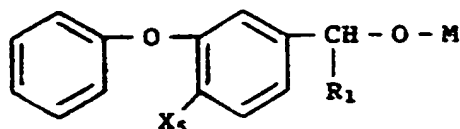
The pour-on method of application is known. In this method, a low volume of a concentrated parasitocidal formulation is applied as a line or spot to the head or back of the animal. This gives protection over the whole animal. The pour-on method is very advantageous to the farmer or grazier since it allows the animal to be treated in a matter of seconds and requires a minimum of labour, thereby keeping costs down. The pour-on method is well established for cattle and a pour-on formulation containing the organophosphorus compound famphur is commercially available under the trade mark "Warbex".

However, attempts by the applicant over a long period to develop a corresponding pour-on for sheep have hitherto met with disappointing results. As shown in the comparative

tests hereafter, a large number of established parasiticides proved ineffective when applied as pour-ons to sheep. This difference in activity is surprising since the previously widely-held view was that the parasiticide worked systemically, i.e. passed through the skin into the bloodstream. If such a mechanism were correct the difference in activity between cattle and sheep is difficult to explain. Thus, up to the present no pour-ons had been available for the treatment of sheep (particularly merino sheep), which could be used as a substitute for conventional dipping or spraying.

The present invention is based on the discovery that a class of known insecticides, the pyrethroids, are surprisingly effective in controlling sheep ectoparasites when applied by the pour-on method. The pyrethroids are synthetic analogues of the naturally occurring pyrethrins and are typically described in British Patent Specification number 1,413,491.

In particular, the present invention provides an especially advantageous pour-on formulation for localised application, which comprises a pyrethroid of the formula







of large numbers of sheep is facilitated.

Without wishing to be limited by any theoretical mode of action, it is believed that the pyrethroid acts superficially and is not dermally and systemically absorbed. It is therefore surprising that protection over the entire sheep is attainable from a localised application.

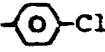
The pyrethroid is preferably selected from the group of light stable pyrethroids. Deltamethrin (also known as decamethrin) is preferred and is a solid under normal conditions. Suitable pyrethroids are disclosed in Tables I to III. The formulae encompass all isomers and mixtures thereof.

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TABLE I

$  \begin{array}{c}  \text{M} = -\text{CC}-\text{CH}-\text{CH}-\text{CH}=\text{C} \begin{array}{l} \nearrow \text{X}_1 \\ \searrow \text{X}_2 \end{array} \\  \quad \quad \quad \diagdown \quad \diagup \\  \quad \quad \quad \text{C} \\  \quad \quad \quad \diagup \quad \diagdown \\  \quad \quad \quad \text{CH}_3 \quad \text{CH}_3  \end{array}  $							
No.	X <sub>1</sub>	X <sub>2</sub>	X <sub>3</sub>	X <sub>4</sub>	X <sub>5</sub>	R <sub>1</sub>	trivial name
1	Cl	Cl	--	--	H	H	permethrin
2	CH <sub>3</sub>	CH <sub>3</sub>	--	--	H	H	phenothrin
3	Br	Br	--	--	H	CN	deltamethrin
4	Cl	Cl	--	--	H	CN	cypermethrin
5	Cl	CF <sub>3</sub>	--	--	H	CN	cyhalothrin
6	Cl		--	--	F	CN	flumethrin
7	Cl	Cl	--	--	F	CN	cyfluthrin
8	CH <sub>3</sub>	CH <sub>3</sub>	--	--	H	CN	cyphenothrin

### TABLE II

$$M = -CO-CH-\underset{\begin{array}{c} \diagdown \\ C \\ \diagup \end{array}}{CH}-\overset{\begin{array}{c} \diagup \\ CH \\ \diagdown \end{array}}{CH}-CH-\overset{\begin{array}{c} X_1 \\ | \\ X_2 \end{array}}{C}$$

$\begin{array}{cc} & X_3 \\ & | \\ CH_3 & CH_3 \end{array}$

No.	X <sub>1</sub>	X <sub>2</sub>	X <sub>3</sub>	X <sub>4</sub>	X <sub>5</sub>	R <sub>1</sub>	trivial name
9	Br	Br	Br	Br	H	CN	tralomethrin
10	Cl	Cl	Br	Br	H	CN	tralomethrin

### TABLE III

$$\begin{array}{c}
 M = -CO-CH-R_2 \\
 | \\
 CH \\
 / \quad \backslash \\
 CH_3 \quad CH_3
 \end{array}$$

It is a particular advantage of the present method that only small volumes of pyrethroid or pyrethroid-containing formula need to be applied. Depending on the size of the sheep, the volume applied will generally lie in the range 2 to 15 ml per sheep.

Depending on the efficacy of the particular pyrethroid employed, the formulation generally contains from 0.1 to 500, preferably 1 to 250 mg/ml of the pyrethroid. Moreover, the pyrethroid is preferably applied to the sheep in the application of from 1 to 500, preferably 1.5 to 250 mg/kg body weight.

The formulation may be applied to full-woolled or sheared sheep. However, higher doses are required for full-woolled sheep.

Diethylene glycol mono-n-butyl ether (i.e. 2-(2-butoxyethoxy)-ethanol) has been found to be particularly useful. It has minimal adverse effect on the skin in terms of the mild epidermal shedding seen with other solvents in some sheep.

Paraffin oils, vegetable oils, e.g. corn oil, peanut oil, castor oil, olive oil, can be added as viscosity modifiers and co-solvents.

Alkylamides and esters of fatty acids are useful formulation adjuncts e.g. n-butyl oleate, N,N-dimethyl oleamide and isopropyl myristate (IPM).

It has been found that the inclusion of an antioxidant such as 2,6-ditert-butyl-4-cresol (BHT) or 2-tert-butyl-4-

methoxyphenol (BHA) has a useful stabilising effect.

The present invention will now be illustrated with reference to comparative tests showing the lack of activity of a large number of conventional insecticides, and with  
5 reference to specific examples illustrating the present invention.

(I) COMPARATIVE TESTS

The effectiveness of a number of known insecticides in  
10 controlling sheep lice using pour-on formulations was assessed. A summary of the active agents and dose rates is given in Table 1.

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TABLE 1

Chemical	Pour-on (mg/kg)
chlorfenvinphos	100
maldison	250
carbaryl	100
dimethoate	100
dioxathion	100
ethion	100
fenitrothion	100
trichlorphon	100
famphur	50, 100
ronnel	100
crotoxyphos	100
bendiocarb	100
bromophos ethyl	100
dichlofenthion	100
crufomate	100
naled	100

All the pour-on treatments were formulated in a solvent system containing xylene, cyclohexanone and corn oil.

A total of 18 groups of lice-infested merino sheep divided into control (1) and treatment groups (17) were selected and treated according to Table 1.

No pour-on treatment had any significant effect on existing lice burdens.

### (II) TREATMENT OF SHEEP WITH PYRETHROIDS

A variety of pyrethroids were evaluated in the control of lice and keds on merino sheep, when applied by a liquid pour-on formulation. Tests 2, 3 and 5 include use of formulations according to the present invention, the remaining results are given as background information.

#### Test 1 (xylene-cyclohexanone-corn oil solvent)

Forty-eight merino sheep, half carrying full-wool and half carrying one month's wool, with significant louse infestations, were allocated equally into four groups of six animals.

Treatments, with Formulations comprising a xylene (55 wt %), cyclohexanone (30 wt %), corn oil (15 wt %) solvent system were made as follows:

Group 1	deltamethrin	10 mg/kg	10 mg/ml formulation
Group 2	deltamethrin	50 mg/kg	50 mg/ml formulation
Group 3	permethrin	100 mg/kg	100 mg/ml formulation
Group 4	permethrin	250 mg/kg	250 mg/ml formulation.

On full-woolled sheep, partings were made along the backline to place the formulation at skin level. After treatment the various groups, each with three full-woolled and three short-woolled sheep, were held in separate pens, remote from each other.

Post-treatment lice examinations were made at 1, 3 and 7 weeks, to assess the effects of the various treatments on the louse populations.

At seven weeks, groups 1 and 2 were run with a mob of fifteen infestor sheep, carrying considerable lice infestations, to gauge the persistence of deltamethrin. Further examinations were made at 9 weeks but subsequent examinations were prevented by wet weather.

#### Results

The results of the pre-treatment and post-treatment lice examinations are shown in Table 2 and are outlined below.



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GROUP 1	full wool	Infestations fell rapidly to extremely low levels and persisted at these low levels throughout the trial.
deltamethrin (10 mg/kg)	short wool	One light infestation was eradicated by Week 1. Moderate to heavy infestations were eradicated by Week 7.

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GROUP 2	full wool	At one week, two newly emerged lice were found in matted wool on one animal, only after an exhaustive search. No lice were seen on the other two animals. At Week 3 an exhaustive search of each animal revealed one or two newly emerged lice. No lice were found at Week 7 or at Week 9, after a fourteen-day challenge period.
deltamethrin (50 mg/kg)	short wool	No lice were seen at any examination after treatment.

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GROUP 3	full wool	Infestations were markedly reduced but were maintained at low levels throughout the trial.
permethrin (100 mg/kg)	short wool	Infestations were reduced to extremely low levels but lice were still present at Week 7.

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GROUP 4	full wool	Infestations were greatly reduced on two out of three sheep but persisted at low levels until Week 7. Lice were eradicated on the third animal by Week 7.
permethrin (250 mg/kg)	short wool	Light infestations were drastically reduced at Week 1 and eradicated at Week 3.

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In the following tables, the numbers represent the total number of lice detected in twenty partings of the wool of the sheep, and

L = light infestation  
M = moderate infestation  
H = high infestation

0 = no lice present  
+ = lice present.

TABLE 2

(First Three Sheep per Group Carrying Full-Wool,  
Second Three Carrying One Month's Wool)

Group	Sheep No.	Pre-Treatment	Week 1	Week 3	Week 7	Week 9	Comments
GROUP 1 deltamethrin (10 mg/kg)	B 34	H	13/20	24/20	16/20	2/20	
	B 882	H	L-M	L-M	2/20*	8/20*	*One heavy patch found
	O 800	L	0	0	0	0	in neck fold
	B 28	M-H	14/20	0	0	0	
	Y 749	M-H	3/20	1/20	0	0	
GROUP 2 deltamethrin (50 mg/kg)	B 883	M-H	0	5/20	0	0	
	G 790	H	2/20**	1/20	0	0	
	Y 840	M-H	0	2/20	0	0	**Found in matted wool
	B 44	M-H	0	0	0	0	
	Y 830	L-M	0	0	0	0	
	Y 738	M	0	0	0	0	
GROUP 3 permethrin (100 mg/kg)	B 50	H	L	L	L		
	Y 835	H	M	M-H	M-H		
	Y 833	H	L	L	19/20		
	B 27	M-H	20/20	9/20	24/20		
	B 49	M	17/20	6/20	11/20		
	Y 744	L-M	7/20	3/20	4/20		
GROUP 4 permethrin (250 mg/kg)	B 887	H	12/20	7/20	3/20		
	B 38	L-M	7/20	0	0		
	B 42	H	L-M	L-M	L		
	B 35	L	1/20	0	0		
	B 29	L	1/20	0	0		
	Y 991	L	1/20	0	0		
CONTROLS	47	L-M	M-H	M	L	L	
	877	H	H	H	H	H	
	742	H	H	H	M-H	M-H	
	754	L	L-M	L-M	L	L-M	
	37	M	M	L	L	L-M	
	736	L-M	M	L-M		died	

## Test 2

The results of the evaluation of deltamethrin on recently sheared merino sheep using xylene and DGBE-based solvent systems are given in Tables 3 and 4. The results of the untreated control group are given in Table 5.

The xylene-based solvent system is the same as that given in Test 1.

The DGBE-based solvent system had a composition as follows:

10	diethylene glycol mono-n-butyl ether (DGBE)	85	wt %
	isopropyl myristate (IPM)	15	wt %
	2,6-ditert-butyl-4-cresol (BHT)	2.5	g/l.

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TABLE 3  
Xylene-Based Solvent\*

Delta-methrin (g/l)	Group	Sheep No.	Body-weight (kg)	Dose (ml)	Post-Treatment Inspections		Challenge Inspections (Group 1 and Group 2)		
					week 3	week 6	week 10	week 12	week 14
8.0	GROUP 1 (a)	51	50	6.3	0	0	0	0	0
	1 mg/kg	90	46	5.8	0	0	0	0	2
	1 ml/8 kg	126	44	5.5	0	0	0	0	0
4.0	GROUP 1 (b)	52	44	11.0	0	0	0	lashed	
	1 mg/kg	55	48	12.0	0	0	0	0	
	1 ml/4 kg	139	43	10.8	0	0	0	0	
16.0	GROUP 2 (a)	54	50	6.3	0	0	0	0	2
	2 mg/kg	112	44	5.5	0	0	0	0	1
	1 ml/8 kg	127	46	5.8	0	0	0	0	1
8.0	GROUP 2 (b)	53	44	11.0	0	0	slaughtered (injury)		
	2 mg/kg	88	48	12.0	0	0	0	1	3
	1 ml/4 kg	146	43	10.8	0	0	0	0	2
20.0	GROUP 3 (a)	76	50	6.3	0	0			
	2.5 mg/kg	126	44	5.5	0	0			
	1 ml/8 kg	134	46	5.8	0	0			
10.0	GROUP 3 (b)	67	44	11.0	0	0			
	2.5 mg/kg	75	42	10.5	0	0			
	1 ml/4 kg	102	48	12.0	0	0			
20.0	GROUP 4 (a)	113	50	6.3	0	0			
	3 mg/kg	131	44	5.5	0	0			
	1 ml/8 kg	137	46	5.8	0	0			
12.0	GROUP 4 (b)	69	44	11.0	0	0			
	3 mg/kg	84	42	10.5	0	0			
	1 ml/4 kg	143	48	12.0	0	0			
32.0	GROUP 5 (a)	61	49	6.1	0	0			
	4 mg/kg	141	44	5.5	0	0			
	1 ml/8 kg	147	46	5.8	0	0			
16.0	GROUP 5 (b)	71	44	11.0	0	0			
	4 mg/kg	110	42	10.5	0	0			
	1 ml/4 kg	118	47	11.8	0	0			
40.0	GROUP 6 (a)	58	45	5.6	0	0			
	5 mg/kg	68	49	6.1	0	0			
	1 ml/8 kg	83	43	5.4	0	0			
20.00	GROUP 6 (b)	80	44	11.0	0	0			
	5 mg/kg	124	47	11.8	0	0			
	1 ml/4 kg	125	42	10.5	0	0			

\*Figures shown in "week" columns are the number of lice seen in twenty wool particles.

TABLE 4  
DCBE-Based Solvent\*

Delta-methrin (g/l)	Group	Sheep No.	Body-weight (kg)	Dose (ml)	Post-Treatment Inspections		Challenge Inspections (Group 1 and Group 2)		
					week 3	week 6	week 10	week 12	week 14
8.0	GROUP 1 (c)	60	45	5.6	0	0	0	1	1
	1 mg/kg	73	49	6.1	0	0	0	3	0
	1 ml/8 kg	85	43	5.4	0	0	0	1	1
4.0	GROUP 1 (d)	78	41	10.3	<1/20	0	0	4	1
	1 mg/kg	61	44	11.0	0	0	1	0	1
	1 ml/4 kg	129	47	11.8	0	0	0	0	0
16.0	GROUP 2 (c)	62	45	5.6	0	0	0	3	2
	2 mg/kg	74	49	6.1	0	0	0	1	1
	1 ml/8 kg	96	43	5.4	0	0	slaughtered (injury)		
8.0	GROUP 2 (d)	18	41	10.3	0	0	0	1	0
	2 mg/kg	89	44	11.0	0	0	0	1	1
	1 ml/4 kg	132	47	11.8	0	0	0	1	2
20.0	GROUP 3 (c)	86	49	6.1	<1/20	0			
	2.5 mg/kg	107	45	5.6	0	0			
	1 ml/8 kg	114	43	5.4	0	0			
10.0	GROUP 3 (d)	91	41	10.3	0	0			
	2.5 mg/kg	94	44	11.0	0	0			
	1 ml/4 kg	144	47	11.8	0	0			
24.0	GROUP 4 (c)	108	45	5.6	0	0			
	3 mg/kg	117	43	5.4	0	0			
	1 ml/8 kg	120	49	6.1	0	0			
12.0	GROUP 4 (d)	56	40	10.0	0	0			
	3 mg/kg	57	46	11.5	0	0			
	1 ml/4 kg	97	44	11.0	0	0			
32.0	GROUP 5 (c)	119	43	5.4	0	0			
	4 mg/kg	128	49	6.1	0	0			
	1 ml/8 kg	135	45	5.6	0	0			
16.0	GROUP 5 (d)	66	40	10.0	0	0			
	4 mg/kg	70	46	11.5	0	0			
	1 ml/4 kg	96	44	11.0	0	0			
40.0	GROUP 6 (c)	133	43	5.4	0	0			
	5 mg/kg	136	49	6.1	0	0			
	1 ml/8 kg	145	45	5.6	0	0			
20.0	GROUP 6 (d)	72	40	10.0	0	0			
	5 mg/kg	87	46	11.5	0	0			
	1 ml/4 kg	101	44	11.0	0	0			

\*Figures shown in "week" columns are the number of lice seen in twenty wool partings.

TABLE 5

Results of Examinations of  
Shorn Untreated Control Group\*

Untreated Controls			
Sheep No.	Body- weight (kg)	Week 3	Week 6
65	51	10	10
77	56	9	8
79	52	17	15
82	38	24	31
95	54	18	29
104	28	37	35
105	52	20	8
111	29	24	23
116	44	10	16
122	39	22	18
123	36	19	18
130	35	18	17

\*Figures show the number of lice  
seen in twenty wool partings.

### 20 Test 3 (varying solvent systems)

Table 6 gives the results for formulations of deltamethrin in a variety of other solvent systems when applied to recently sheared merino sheep.

TABLE 6

## Various Solvent Systems

Sheep No.	Body wt. (kg)	Dose (ml)	Pre-treat. ment	Week 4	Week 6	Week 8	Formulations
140	27	6	91	0	0	0	10 g/l deltamethrin in xylene system of Test 1
174	27	6	66	0	0	0	
175	26	6	30	1	0	0	
172	17	9	47	1	0	0	10 g/l deltamethrin 2.5 g/l BHT to 1 litre with cyclohexanone containing 50 ppm SUDAN RED IV
178	33	8	90	0	0	0	
180	34	8	47	0	0	0	
131	25	6	51	0	0	0	10 g/l deltamethrin 2.5 g/l BHT 50 ppm SUDAN RED IV DCBP/cyclohexanone (65:35 w/w) to 1 litre
132	29	6	34	0	0	0	
138	28	6	87	0	0	0	
142	32	8	73	0	0	0	10 g/l deltamethrin 100 g/l mineral oil 2.5 g/l BHT 50 ppm SUDAN RED IV cyclohexanone to 1 litre
149	24	6	47	0	0	0	
181	31	8	27	0	0	0	
164	36	5	117	0	0	0	10 g/l deltamethrin 100 g/l mineral oil 2.5 g/l BHT 50 ppm SUDAN RED IV diethylene glycol mono-n-butyl ether (DCBE) to 1 litre
165	33	8	47	0	0	0	
177	30	4	27	0	0	0	
143	31	8	90	1	0	0	10 g/l deltamethrin 2.5 g/l BHT 50 ppm SUDAN RED IV dipropylene glycol monomethyl ether (DPH) to 1 litre
155	21	6	44	1	0	0	
162	25	6	75	1	0	0	
137	29	6	60	0	0	0	10 g/l deltamethrin 2.5 g/l BHT 100 g/l acetylated lanoline alcohols cyclohexanone to 1 litre
163	28	6	72	0	0	0	
169	21	6	39	0	0	0	
129	29	-	14	14	8	17	Controls
130	23	-	18	28	14	22	
154	25	-	-	171	47	72	
160	36	-	17	8	8	24	
171	30	-	17	29	24	20	

#### Test 4 (varying pyrethroids)

The efficacy of a variety of different pyrethroids applied as liquid pour-on formulations to merino sheep was determined. The results are given in Table 7. A backline application was made within 24 hours of shearing. All formulations used the xylene-based solvent system given in Test 1, except flumethrin which was formulated as a miscible oil formulation but which was diluted with the xylene-based solvent to achieve the lower concentrations.

The results show all the pyrethroids tested to be effective, although at the dosages used phenothrin and flumethrin did not give complete eradication.

#### Test 5 (effect of deltamethrin against keds)

The efficacy of deltamethrin against infestations of merino sheep with keds (*Melophagus ovinus*) was determined by applying 8 ml of deltamethrin in the xylene-based solvent system given in Test 1 as a backline treatment to twenty newly shorn sheep. Twenty further sheep were treated in the same way with deltamethrin in the DGBE-based solvent system given in Test 2. The concentration of deltamethrin was 10 g/l.

All forty sheep were re-examined 10 weeks after treatment and no live keds were found.



**TABLE 7**  
**Control of the Sheep-Biting Louse**  
**by a Number of Pyrethroids**

Compound / Dose / Formulation	Sheep No.	Result (No. of Lice)
<b>CYPERMETHRIN</b>		
5 mg/kg	792	3
(1 ml / 5 kg - 25 g/l formulation)	767	7
	732	26
50 mg/kg	756	3
(1 ml / 5 kg - 250 g/l formulation)	746	3
	733	0 (14/10 - D)
<b>PHENOTHRIN</b>		
25 mg/kg	721	8
(1 ml / 5 kg - 125 g/l formulation)	765	23
	727	3
400 mg/kg	724	8
(4 ml / 5 kg - 500 g/l formulation)	779	6
	753	19
<b>FENVALERATE</b>		
10 mg/kg	744	9
(1 ml / 5 kg - 50 g/l formulation)	740	3
	769	2 (14/10 - D)
100 mg/kg	766	0
(2 ml / 5 kg - 250 g/l formulation)	770	0
	730	0
<b>FLUMETHRIN</b>		
0.5 mg/kg	783	21
(1 ml / 5 kg - 2.5 g/l formulation)	725	10
	719	1
12-16 mg/kg	722	0
(25 ml / 30-40 kg - 20 g/l formulation)	755	5
	748	7
<b>CONTROLS</b>		
no treatment	741	64
	737	52
	764	83
	754	53
	758	121
	723	55

D = died between 14/10 and 21/10

Test 6 (time to take effect)

The time for the pyrethroid to fully clear the merino sheep following backline application of the liquid formulation was investigated and the results are shown in Table 8.

- 5 These demonstrate that the pyrethroid takes a finite period to completely clear the sheep of lice. However, the sheep are substantially cleared within 15 days. The effect is also demonstrated in certain of the preceding Tables.

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TABLE 8

Process of Reduction in Lice Numbers  
Following Pyrethroid Backline Treatment

Group	Sheep No.	L i c e   S c o r e					
		0	7	9	15	35	42
Cypermethrin 50 mg/kg	756	>20	7	3	0	2I	0
	746	>20	7	2	5	2I	0
	733	>20	9	3	0	0	0
Fenvalerate 100 mg/kg	766	>20	2	2	3	0	0
	770	>20	6	1	0	0	0
	730	>20	2	2	2	1I	0
Flumethrin 12-16 mg/kg	722	>20	10	-	8	4I	0
	755	>20	19	-	10	18I	3I, 2A
	748	>20	12	-	4	7I, 2A	4I, 3A
Controls	741	>20	-	-	14	-	64(18)
	737	>20	-	-	15	-	52(18)
	764	>20	-	-	16	-	83(19)
	754	>20	-	-	10	-	53(15)
	758	>20	-	-	22	-	121(19)
	723	>20	-	-	20	-	55(13)

I = immature lice  
A = adult lice

(III) FORMULATIONS ACCORDING TO THE PRESENT INVENTION

Example 1

10.1 g of technical deltamethrin (989 g active per kg) was  
5 dissolved in a solvent consisting of:

diethylene glycol monobutyl ether

BHT antioxidant 2500 ppm

Sudan Red IV 50 ppm

and the volume adjusted to one litre with the same solvent  
10 to give a solution containing 10 g/l deltamethrin. *The antioxidant and Sudan Red dye are expressed as ppm of the total solvent.*

Example 2

10.1 g of technical deltamethrin (989 g active per kg) was  
dissolved in a solvent blend containing:

15 cyclohexane 50% by weight  
diethylene glycol monobutyl ether 50% by weight  
BHT antioxidant 2500 ppm  
Solvent Blue No. 36 50 ppm

and the volume adjusted with the same solvent blend to give  
20 a solution containing 10 g/l deltamethrin.

Example 3

10.1 g of technical deltamethrin (989 g active per kg) was  
dissolved in a solvent blend containing:

25 diethylene glycol monobutyl ether 85-90% by weight  
isopropyl myristate 10-15% by weight  
BHT antioxidant 2500 ppm  
Sudan Red IV 50 ppm



and the volume adjusted with the respective solvent blend to  
give a solution containing 10 g/l deltamethrin.

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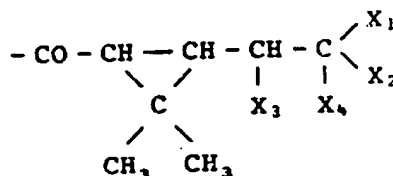
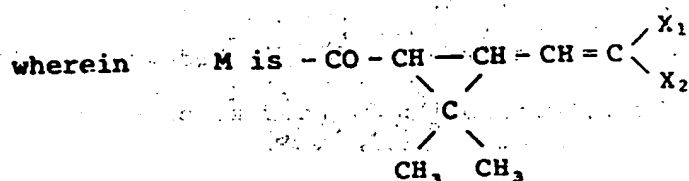
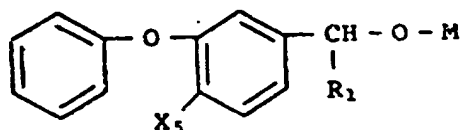
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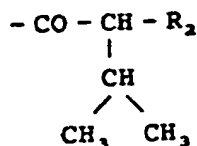
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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A pour-on formulation for localised application, which comprises a pyrethroid of the formula



or



and wherein X<sub>1</sub> to X<sub>4</sub> are independently selected from halo, C<sub>1</sub>-C<sub>4</sub> alkyl, halogen-substituted C<sub>1</sub>-C<sub>4</sub> alkyl, and halogen-substituted phenyl;

X<sub>5</sub> is -H or halo;

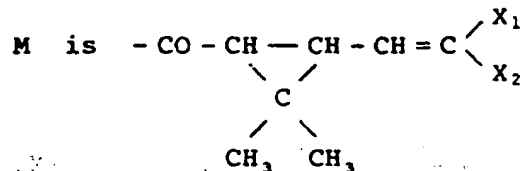
R<sub>1</sub> is -H or cyano; and

R<sub>2</sub> is halogen-substituted phenyl;

in admixture with diethylene glycol mono-butyl ether.

2. A formulation according to claim 1 wherein the pyrethroid is a light-stable pyrethroid.

3. A formulation according to either preceding claim wherein



$\text{X}_1$  and  $\text{X}_2$  are independently selected from chloro and bromo; and

$\text{X}_3$  is -H or halo; and

$\text{R}_1$  is -H or cyano.

4. A formulation according to claim 1 wherein the pyrethroid is selected from permethrin, phenothrin, cyfluthrin, cyphenothrin, tralomethrin, tralocythrin and fenvalerate (all as herein defined).

5. A formulation according to claim 1 wherein the pyrethroid is deltamethrin (as herein defined).

6. A formulation according to claim 1 wherein the pyrethroid is cyhalothrin (as herein defined).

7. A formulation according to claim 1 wherein the pyrethroid is flumethrin (as herein defined).

8. A pour-on formulation for localised application, which comprises cypermethrin (as herein defined) in admixture with diethylene glycol mono-butyl ether.

9. A formulation according to any preceding claim wherein the formulation contains 1 to 250 mg/ml of the pyrethroid.

10. A formulation according to any preceding claim which further comprises cyclohexanone.

11. A formulation according to any one of claims 1 to 9 which further comprises an ester of a fatty acid. 9 which further comprises an ester of a fatty acid.

12. A formulation according to claim 11 wherein the ester is isopropyl myristate. A formula

13. A formulation according to any preceding claim which includes a dyestuff.

14. A pour-on formulation substantially according to any one of Examples 1 to 3.

DATED this 2nd day of December, 1983

WELLCOME AUSTRALIA LIMITED  
By their Patent Attorney  
GRIFFITH HASSEL & FRAZER



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